

Metal-Free Catalytic Oxidation of Sulfides to Sulfoxides with Ammonium Nitrate, Ammonium Hydrogen Sulfate and Ammonium Bromide as Catalyst

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A oxidação catalítica geral e sem o uso de metais, de sulfetos alifáticos e aromáticos aos seus sulfóxidos correspondentes *via* combinação de nitrato de amônio (NH₄NO₃), hidrogenossulfato de amônio suportado em sílica gel (NH₄HSO₄-SiO₂) e uma quantidade catalítica de brometo de amônio (NH₄Br) na presença de SiO₂ aquoso (50%, m/m) foi investigada. As reações ocorreram em meio heterogêneo e seletivamente em curtos tempos de reação, em CH₂Cl₂ a temperatura ambiente. Este procedimento é simples e eficiente comparado a outros métodos relatados.

A general and metal-free catalytic oxidation of aliphatic and aromatic sulfides to their corresponding sulfoxides *via* combination of ammonium nitrate (NH₄NO₃), supported ammonium hydrogen sulfate on silica gel (NH₄HSO₄-SiO₂) and a catalytic amount of ammonium bromide (NH₄Br) in the presence of wet SiO₂ (50%, w/w) has been investigated. The reactions were carried out heterogeneously and selectively in short reaction times in CH₂Cl₂ at room temperature. This protocol is mild and efficient compared to other reported methods.

Keywords: sulfides, sulfoxide, ammonium hydrogen sulfate (NH₄HSO₄), ammonium nitrate (NH₄NO₃), ammonium bromide (NH₄Br), homoselectivity

Introduction

The chemoselective oxidation of sulfides to their corresponding sulfoxides is of interest for organic chemists, both for fundamental research and for a variety of applications. Sulfoxides are valuable synthetic intermediates for the synthesis of chemically and biologically significant molecules.¹⁻³ Sulfoxides are also valuable materials in C-C bond-forming^{4,5} and molecular rearrangements.⁶⁻⁸ Additionally some of biologically active sulfoxides play an important role as therapeutic agents such as anti-ulcer,⁹⁻¹¹ antibacterial,¹² anti-atherosclerotic,^{13,14} among others. Although a wide variety of oxidizing systems has been applied for the oxidation of sulfides to the sulfoxides such as H₂O₂/silica sulfuric acid,¹⁵ urea hydrogen peroxide (UHP)/Mn(III),¹⁶ Me-IBX,¹⁷ H₂O₂/VO(acac)₂,¹⁸ N-bromosuccinimide,¹⁹ H₂O₂/NBS,²⁰ H₂O₂/Cr(III),²¹ 1-benzyl-4-aza-1-azonia-bicyclo[2.2.2]octane tribromide,²² BF₄-based ionic liquid/UHP,²³ H₂O₂/1,1,1-trifluoroacetone,²⁴ some of these methods still suffer from some drawbacks like overoxidation to sulfones,

low selectivity, low yields of products, tedious work-up, toxicity, and expensive reagents or catalysts.

In the last few years, heterogeneous reagents and catalysts are used increasingly in organic functional group transformation.²⁵⁻²⁸ The development of efficient and new catalytic systems for various organic transformations is an active research area with the aim to develop milder reaction conditions.²⁹ Finding molecules which are able to catalyze the reaction between others is an important contribution of molecular chemists to increase the efficiency of chemical reactions whereby our daily life based on consumption of chemicals is shifted closer to an ecologically and economically tolerable equilibrium with our environment.³⁰

Results and Discussion

Recently we have introduced different approaches for the *in situ* generation of bromonium ion (Br⁺), which effectively applied for the oxidation of different types of organic compounds.³¹⁻³⁶ In continuation of this investigation we decided to explore catalytic and metal-free media for the *in situ* generation of Br⁺. Meanwhile we were interested to use ammonium nitrate (NH₄NO₃) as very cheap, nontoxic

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and commercially available oxidizing material. Ammonium nitrate is used in fertilizer industry and as an explosive in mining operations. It has been also used widely in different organic transformations such as: cleavage of THP ethers, acetals and acetonides,³⁷ nitration of arenes,³⁸ dethioacetalization,³⁹ coordination of ammonium nitrate to crown ethers.⁴⁰

However, the low oxidizing power of ammonium nitrate is the main drawback to its application. Therefore we decide to activate this reagent with supported ammonium hydrogen sulfate on silica gel ($\text{NH}_4\text{HSO}_4\text{-SiO}_2$). Therefore a mixture of NH_4NO_3 , $\text{NH}_4\text{HSO}_4\text{-SiO}_2$ (50%, w/w) and catalytic amounts of NH_4Br in the presence of wet SiO_2 (50%, m/m), as metal free catalytic media, was combined for the *in situ* generation of Br^+ . Consequently, we disclosed a new heterogeneous catalytic protocol for the chemo and homoselective oxidation of sulfides to the sulfoxides using combination of ammonium nitrate, ammonium hydrogen sulfate and wet SiO_2 (50%, w/w) in the presence of catalytic amounts of NH_4Br .

Obviously, solvent plays an important role in organic transformations, and hence it was decided to investigate the solvent effect and also find an appropriate solvent for the oxidation of sulfides. However, we screened different solvents for the oxidation of sulfides. However, we screened different solvents for the oxidation of dibenzyl sulfide, as a typical example. The oxidation of dibenzyl sulfide was carried out using a mixture containing 1mmol of dibenzyl sulfide, NH_4NO_3 (1.2 mmol), $\text{NH}_4\text{HSO}_4\text{-SiO}_2$ (50%, w/w) (1.2 mmol), NH_4Br (0.02 mmol) and 0.2 g of wet SiO_2 (50%, w/w) in 5 mL of solvent at room temperature. As is evident from Table 1 oxidation reaction proceeds more rapidly and more selectively in dichloromethane compared to other solvents.

Eventually, we wish to report here the selective oxidation of wide range of aliphatic and aromatic sulfides **1** to the corresponding sulfoxides **2** using NH_4NO_3 I, supported

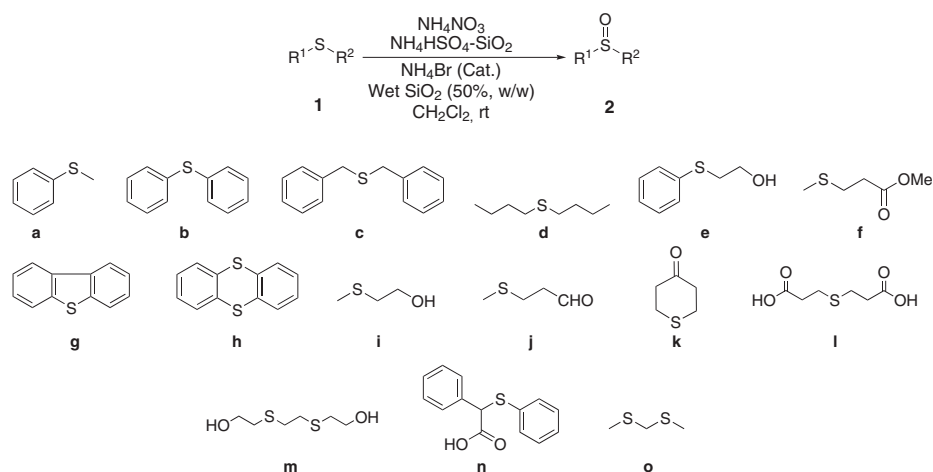
Table 1. Oxidation of dibenzyl sulfide using NH_4NO_3 , $\text{NH}_4\text{HSO}_4\text{-SiO}_2$ (50%, w/w) and catalytic amounts of NH_4Br in the presence of wet SiO_2 (50%, w/w) in different solvents at room temperature^a

Entry	Solvent	time / min	Yield / (%) ^b
1	Acetonitrile	30	98
2	Acetone	480	--- ^c
3	Chloroform	35	90
4	Dichloromethane	20	98
5	<i>n</i> -Hexane	162	--- ^d
6	Ethanol	480	--- ^c
7	Methanol	480	--- ^c
8	Ethyl acetate	80	96

^aSubstrate : NH_4NO_3 : $\text{NH}_4\text{HSO}_4\text{-SiO}_2$: NH_4Br : wet SiO_2 = 1 mmol : 1.2 mmol : 1.2 mmol : 0.02 mmol : 0.2 g. ^bIsolated yield. ^cNo reaction. ^dReaction was complete but impurity of sulfone was observed.

ammonium hydrogen sulfate on silica [$\text{NH}_4\text{HSO}_4\text{-SiO}_2$ (50%, w/w)] II and catalytic amounts of NH_4Br III in the presence of wet SiO_2 (50%, w/w) in dichloromethane at room temperature with good to excellent yields (Scheme 1 and Table 2).

NH_4Br is the catalytic part of this oxidizing system. Therefore to investigate the catalytic role of NH_4Br dibenzyl sulfide was subjected to the oxidation reaction in the absence of catalyst. However, no sulfoxide was observed after 3 h (Table 1, entry 4). Also the necessity of wet SiO_2 (50%, w/w), as source of water, and $\text{NH}_4\text{HSO}_4\text{-SiO}_2$ (50%, w/w) were considered. Therefore to show the role of supported ammonium hydrogen sulfate on silica in this system, oxidation of dibenzyl sulfide was carried out in the absence of this reagent. Interestingly it was observed that the reaction did not proceed in the absence of $\text{NH}_4\text{HSO}_4\text{-SiO}_2$ (Table 1, entry 5). Also is evident from entry 6 of Table 1, that wet SiO_2 is necessary for the described system.



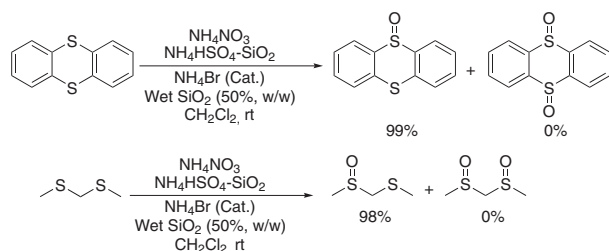
Scheme 1. Catalytic oxidation of sulfides to the corresponding sulfoxides.

Table 2. Oxidation of sulfides **1** to the corresponding sulfoxides **2** using NH_4NO_3 (I), $\text{NH}_4\text{HSO}_4\text{-SiO}_2$ (50%, w/w), (II) and catalytic amounts of NH_4Br (III) in the presence of wet SiO_2 (50%, w/w) in dichloromethane at room temperature

Entry	Substrate	Product	Substrate/Reagents/ Catalyst / mmol ^a			time / min	Yield / (%) ^b
			I	II	III		
1	1a	2a	1.2	1.2	0.02	25	85
2	1b	2b	2	2	0.15	48 h	70 ^c
3	1c	2c	1.2	1.2	0.02	20	98
4	1c	2c	1.2	1.2	---	180	--d,e
5	1c	2c	1.2	---	0.02	180	--e,f
6	1c	2c	1.2	1.2	0.02	180	--e,g
7	1d	2d	1.2	1.2	0.02	20	86
8	1e	2e	1.5	1.5	0.1	165	96
9	1f	2f	1.2	1.2	0.02	15	98
10	1g	2g	1.2	1.2	0.02	50	93
11	1h	2h	2	2	0.1	26 h	99
12	1i	2i	1.2	1.2	0.02	60	86
13	1j	2j	1.2	1.2	0.02	20	73
14	1k	2k	1.2	1.2	0.02	35	98
15	1l	2l	1.2	1.2	0.02	15	45
16	1m	2m	1.2	1.2	0.02	180	20
17	1n	2n	1.2	1.2	0.02	10	85
18	1o	2o	1.2	1.2	0.02	40	98

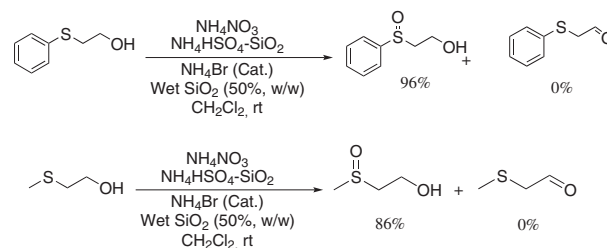
^aSubstrate : wet SiO_2 = 1 mmol : 0.2 g. ^bIsolated yield. ^cGC yield. ^dIn the absence of NH_4Br . ^eNo reaction. ^fIn the absence of $\text{NH}_4\text{HSO}_4\text{-SiO}_2$. ^gIn the absence of wet SiO_2 .

It is of interest to note that the mentioned oxidizing system allowed the homoselective^{31,33} oxidation of thianthrene and bis-(methyl thio)-methane to their monosulfoxide derivatives (Scheme 2, entries 11 and 18).



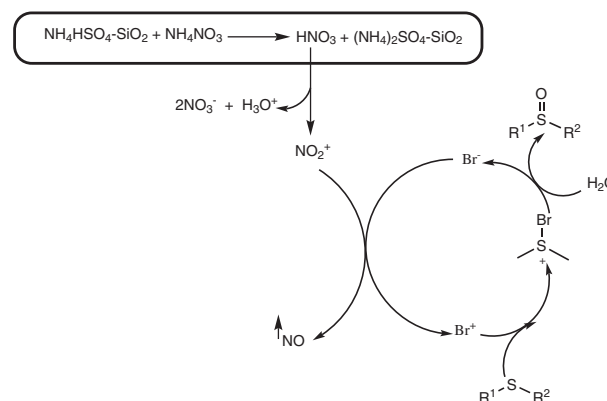
Scheme 2. Homoselective oxidation of thianthrene and bis-(methyl thio)-methane to their monosulfoxide derivatives.

Finally to show the chemoselectivity of the described system, two sulfides containing a hydroxy group were subjected to the sulfoxidation reaction, but alcohol oxidation did not occur under mentioned conditions, and primary hydroxyl group remained intact in the course of the reaction (Table 2, entries 8 and 12, Scheme 3).



Scheme 3. Chemoselective sulfoxidation of 2-(phenylthio) ethanol and 2-(methylthio) ethanol.

A possible mechanism of this oxidizing system is shown in Scheme 4 based on our previously reported works.³¹⁻³⁶



Scheme 4. General mechanism for the oxidation of sulfides to the sulfoxides.

In the first place, NH_4NO_3 reacts with NH_4HSO_4 to produce *in situ* HNO_3 . Subsequently, auto ionization of HNO_3 generates nitronium ion (NO_2^+), which is able to convert bromide ion (Br^-) to bromonium (Br^+). In the last step reaction of bromonium ion with sulfide in the presence of water might generate the corresponding sulfoxide.

In summary herein we report a novel catalytic protocol for the chemo and homoselective oxidation of sulfides to the sulfoxides under metal-free, mild and heterogeneous conditions. This method offers the advantage of shorter reaction times, high selectivity, non toxic conditions, cost effective reagents and catalyst and easy workup. We believe that the present methodology could be an important addition to the existing methodologies.

Experimental

Chemicals were purchased from Fluka, Merck and Aldrich chemical companies. The oxidation products were characterized by comparison of their spectral (IR, ^1H NMR, and ^{13}C NMR) and physical data with authentic samples.

Oxidation of dibenzyl sulfides 1c to dibenzyl sulfoxide 2c using NH₄NO₃, NH₄HSO₄-SiO₂ and NH₄Br as a typical procedure

NH₄NO₃ (0.096 g, 1.2 mmol), NH₄Br (0.0019 g, 0.02 mmol), NH₄HSO₄-SiO₂ (50%, w/w), (0.276 g, 1.2 mmol) and 0.2 g of wet SiO₂ (50%, w/w) were added to a solution of dibenzyl sulfide **1c** (0.214 g, 1 mmol) in CH₂Cl₂ (5 mL). The resulting mixture was stirred at room temperature for 20 min (the reaction progress was monitored by TLC) and then filtered. The residue was washed with CH₂Cl₂ (4×5 mL). Anhydrous Na₂SO₄ (1.5 g) was added to the filtrate and filtered off after 20 min. Finally CH₂Cl₂ was removed and the yield was 0.221 g (98%).

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